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Letter to the Editor

Clarification of ECLAMC/NFP Case Control Study

To the Editor:

We thank Dr. Pelz for his interest in our work. Much of the considerable information he requested was not included in our original correspondence on the assumption that a Letter to the Editor must be brief. However, we will comment as briefly as seems appropriate.

First, Dr. Pelz is correct in pointing out the embarrassing typographical error. The number of other malformed infants reporting NFP use was 327 and not 227; the odds ratio and 95% confidence limits were not provided as well.

Second, most of Dr. Pelz's other queries are best appreciated by recalling the previously published protocol of ECLAMC (the Spanish acronym for Latin American Collaborative Study of Congenital Malformations), which for decades has followed the same case-control design. Information was gathered on every (infant) case with an anomaly, matched to the next like-sex, nonmalformed liveborn. Perusal of the many prior ECLAMC publications will readily verify this group's facility to take into account potential confounding variables and to perform requisite multivariate analyses.

In the current study, we merely added a questionnaire on natural family planning (NFP) use as reported by the mother. The three matching factors (Dr. Pelz's fifth point) were stated clearly: sex of the infant, time of birth, and location of birth. No effort was made to validate NFP use, an onerous effort that would have been beyond the scope of our study. Even if validation had been attempted, results would have been dwarfed in comparison to those being generated concurrently by our cohort study [Simpson et al, 1988; Gray et al., 1995].

Another query relates to numbers of cases and controls differing and being less than 5,000; the ostensible discrepancies merely reflected pertinent data not being available on all cases/controls.

Finally, no one could disagree with Dr. Pelz's general comments about experimental pitfalls of case-control studies (confounders, misclassifications, insufficient power). Our previous publications should reassure Dr. Pelz concerning our sensitivity to these issues.

Since our original letter was published, our sample size increased to an effective total of 5,277 malformed and 5,371 controls; the informative (discordant) number of Down control pairs is now 262 instead of 199. NFP use was reported by 28/262 or 10.69% mothers within the Down syndrome group vs. 16/262 or 6.11% among matched controls. Our odds ratio was 1.84, with 95% confidence interval: 0.99–3.96. This near-significant difference held true when the discordant intrapair method was applied (odds ratio, 2.00; 95% confidence interval, 0.99–4.24). However, the difference was substantially reduced when the odds ratio (OR) was adjusted for maternal age (OR, 1.78; 95% CI, 0.84–3.75); parity (OR, 1.68; 95% CI, 0.87–3.24); maternal educational level (OR, 1.71; 95% CI, 0.86–3.44); or all three variables together (OR, 1.74; 95% CI, 0.83–3.64).

REFERENCES

Gray R, Simpson JL, Kambic RT, Queenan JT, Mena P, Perez A, Barbato M (1995): Timing of conception and the risk of spontaneous abortion among pregnancies during use of natural family planning. Am J Obstet Gynecol 172:1567–1572.

Simpson JL, Gray RH, Queenan JT, Mena P, Perez A, Kambic RT, Tagliabue G, Pardo F, Stevenson WS, Barbato M, Jennings VH, Zinaman MJ, Spieler JM (1988): Pregnancy outcome associated with natural family planning (NFP): Scientific basis and experimental design for an international cohort study. Adv Contracept 4: 247–264.

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